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Short Note

Hexakis{4-[(4'-hydroxybiphenyl-4-yl)ethynyl]phenyl}benzene

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Abstract: A novel polyphenolic backbone, hexakis{4-[(4'-hydroxybiphenyl-4-yl)ethynyl]phenyl}benzene, was synthesised using a common synthetic protocol used for the synthesis of similar polyphenolic compounds.

Keywords: hexaphenylbenzene; phenol

Introduction

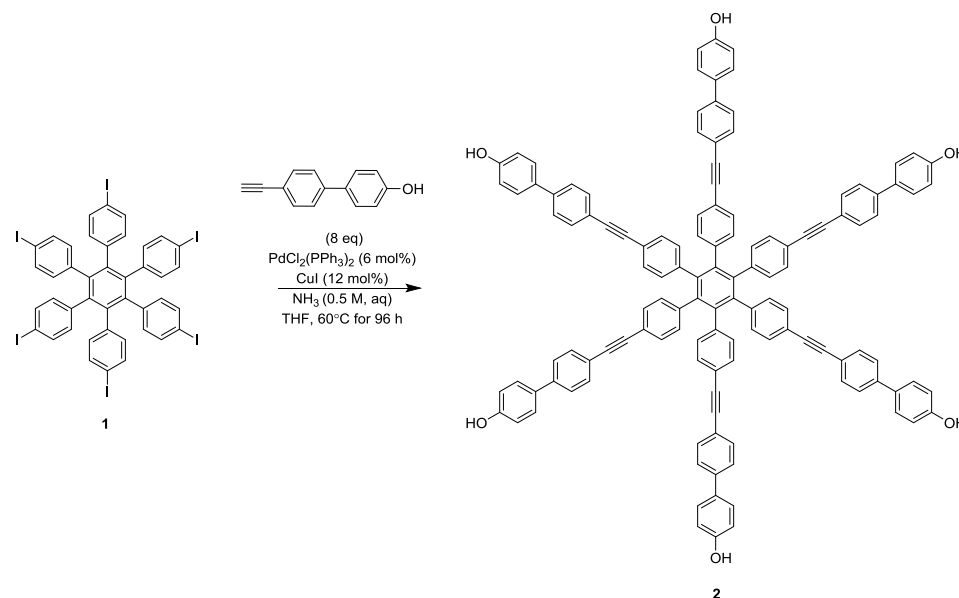
Pulsed Electron Paramagnetic Resonance (EPR) [1,2] techniques have become powerful tools for elucidation of structure and conformational flexibility of complex biological systems [3], such as photosynthetic reaction centres [4], integral membrane proteins [5] and nucleic acids [6]. Pulsed EPR measurements give access to accurate distance measurements of 1.2 to 8 nm between two or more paramagnetic centres, which can be endogenous or chemically introduced by Site-Direct Spin Labelling (SDSL) [3].

Distance measurements in systems containing two spin labels have been proven to be easily accessible and highly accurate and precise [3], however, in multiply labelled complexes these measurements have been proven challenging because of the presence of multi-spin effects. These effects can introduce artefacts hampering data interpretation [7,8]. To quantify and suppress multi-spin effects in pulsed EPR measurements multiply labelled chemical model systems have been synthesised [7,9]. These give access to a better understanding of the phenomenon as they allow measurements to be performed on well-defined systems and under well-defined experimental conditions. Model systems are often much easier to simulate.

Results and Discussion

As a precursor to a novel six-fold labelled multi-spin model systems the intermediate hexaphenol hexakis{4-[(4'-hydroxybiphenyl-4-yl)ethynyl]phenyl}benzene has been isolated.

The synthetic process, reported in Scheme 1, involved the iodination of hexaphenylbenzene [10] using a similar protocol designed by Kobayashi *et al.* [11], followed by Sonogashira cross-coupling, under conditions previously reported by Mohamed Ahmed and Mori [12], and optimised for synthesis of similar polyphenols [9].



Scheme 1. Synthesis of hexaphenol hexakis{4-[(4'-hydroxybiphenyl-4-yl)ethynyl]phenyl}benzene **2**.

Experimental Section

General Methods

Sonogashira cross-couplings were carried out under nitrogen atmosphere using standard Schlenk techniques and freshly distilled solvents. Dry solvents were obtained anhydrous by a SPS alumina column and collected into flame-dried flasks. Solvents for cross-couplings were degassed via the freeze-pump-thaw technique ($\times 3$). ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR experiments (Bruker Avance 500, Fällanden, Switzerland) were performed using a 300 or 500 MHz ^1H 125 MHz ^{13}C at ambient temperature in deuterated solvents. Infrared spectra were recorded with an ATR probe and only characteristics peaks are reported (Shimadzu, Kyoto, Japan). Mass spectrometry data was acquired using matrix-assisted laser desorption/ionisation (MALDI) (Voyager DE-STR, Applied Biosystems, Foster City, CA, USA).

Hexakis{4-[(4'-hydroxybiphenyl-4-yl)ethynyl]phenyl}benzene (**2**)

Hexakis(4-iodophenyl)benzene (**1**) was prepared in modified literature procedures [11]. Hexaphenylbenzene (2 g, 3.7 mmol) was dissolved in dry CH_2Cl_2 (150 mL). To the obtained solution freshly ground iodine (3.8 g, 15 mmol) was added together with [bis-(trifluoroacetoxy)iodo] benzene (6.4 g, 15 mmol); 3.2 g was added just after addition of iodine and the remaining half was added after

30 min. The obtained mixture was left stirring in the dark under nitrogen atmosphere overnight. Hexane was added to the yellow solution to encourage precipitation. The solids were isolated by filtration. The obtained solids were dissolved in chloroform; the solution was washed with 5% sodium bisulfite aqueous solution followed by water and brine. The organic layer was dried over sodium sulfate and solvents removed under reduced pressure. The obtained solids were recrystallized from chloroform to give **1** as a white solid (0.35 g, 51 %) [11,13].

Hexakis(4-iodophenyl)benzene (0.1 g, 0.08 mmol) was dissolved in dry THF (10 mL) together with $\text{PdCl}_2(\text{PPh}_3)_2$ (6% mol., 0.003 g, 0.005 mmol). 4'-Ethynyl-[1,1'-biphenyl]-4-ol (0.12 g, 0.62 mmol) was dissolved in a separate flask in dry THF (10 mL). Both solutions were degassed before drop-wise addition of the alkyne solution to the first solution. The new mixture was degassed once more before addition of CuI (12%, 0.01 g, 0.08 mmol). A 0.5 M aqueous ammonia solution (2.5 mL, 1.3 mmol) was added drop-wise to the new mixture, which was left stirring at 65 °C for 4 days. The mixture was taken up in EtOAc and washed with 10% aqueous HCl solution, water and brine. The organic phase was dried over sodium sulfate and solvents removed under vacuum. The obtained solids (0.2 g) were purified via silica column chromatography (10% EtOAc in CH_2Cl_2 , R_f 0.1). The target molecule was isolated as a brown solid (0.07 g, 55%).

FT-IR (ATR): 2916 (m), 2848 (m), 1662 (m), 1589 (m), 1492 (m), 1274 (m), 1172 (m), 1047 (s), 1022 (s), 997 (s), 821 (s).

^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 9.66 (s, 6H), 7.56 (dd, $J = 37.2, 7.2$ Hz, 36H), 7.18 (d, $J = 7.9$ Hz, 12H), 7.01 (d, $J = 8.0$ Hz, 12H), 6.84 (d, $J = 8.3$ Hz, 12H).

^{13}C NMR (126 MHz, DMSO) δ 157.62, 140.27, 132.07, 131.89, 131.54, 131.46, 130.06, 128.83, 128.73, 127.77, 125.93, 119.96, 115.85, 89.81, 89.55.

MS [MALDI] $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{126}\text{H}_{78}\text{O}_6$ 1687.6, found 1687.6.

^1H and ^{13}C NMR spectra are reported in the supplementary materials as Figures S1 and S2 together with MALDI mass spectra as Figures S3 to S5.

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Author Contributions

SV and BEB planned the research, SV performed the research and analysed the data, SV and BEB wrote the paper.

Conflicts of Interest

The authors declare no conflict of interest.

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13. FT-IR (ATR): 1487 (m), 1138 (m), 1058 (m), 1003 (s), 823 (m). ¹H NMR (300 MHz, Chloroform-*d*) δ 7.23 (s, 12H), 6.54–6.39 (m, 12H).
14. ESI and EI mass spectrometry methods did not give the wanted ions. Low resolution MALDI techniques gave the wanted mass peak, however high resolution analysis using MALDI could not

be achieved due to the lack of an appropriate standard. Microanalysis for **2** did not give acceptable results. We attribute this to the hygroscopic nature of the compound. Similar behaviour with respect to microanalysis and mass spectrometry was found for similar compounds bearing several phenol groups (see Ref. 9).

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